

PT fragment, useful for treating malignant disorders such as myeloid
 PT malignancies, autoimmune disorders and myeloproliferative disorders -
 XX
 PS Claim 8; Page 78; 110pp; English.

XX The invention comprises the amino acid and coding sequences of modulator
 CC of antigen receptor signalling (MARS) proteins. The MARS protein is a
 CC putative tumour suppressor gene and exhibits structural and sequence
 CC similarity to the Src-like adaptor protein (SLAP). The MARS DNA and
 CC protein sequences of the invention are useful for the treatment of
 CC myeloid malignancies (e.g. acute myelogenous leukaemia) autoimmune
 CC disorders, immunosuppression, myeloproliferative disorders and
 CC malignancies related to the de-regulation of tyrosine kinases (e.g.
 CC breast cancer). The present amino acid sequence represents a mouse MARS
 CC protein.

XX Sequence 210 AA;

Query Match 100.0%; Score 446; DB 23; Length 210;
 Best Local Similarity 100.0%; Pred. No. 3.9e-50;
 Matches 83; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 WLVGSLREKAEKELLPGNPGAFILRESQTRGYSLSVRLSPASMDRIIRHYRHL 60
 DB 94 WLVGSLREKAEKELLPGNPGAFILRESQTRGYSLSVRLSPASMDRIIRHYRHL 153
 QY 61 DNGWLYISPRLTFFPSLQALVDHY 83
 DB 154 DNGWLYISPRLTFFPSLQALVDHY 176

RESULT 2

AA015457
 ID AA015457 standard; Protein; 261 AA.

XX AA015457;
 AC
 XX
 DT 03-OCT-2002 (first entry)

XX Human modulator of antigen receptor signalling (MARS) protein.

XX Human; gene therapy; modulator of antigen receptor signalling; MARS;
 KW tumour suppressor gene; Src-like adaptor protein; SLAP;
 KW myeloid malignancy; acute myelogenous leukaemia; autoimmune disorder;
 KW immunosuppression; myeloproliferative disorder; breast cancer.

XX Homo sapiens.

XX WO200242452-A2.

XX 30-MAY-2002.

XX 26-NOV-2001; 2001WO-CA01662.

XX 27-NOV-2000; 2000CA-2324663.

XX (HOSP-) HOSPITAL FOR SICK CHILDREN.

XX McGlade JC, Loreto MP;

XX WPI; 2002-566564/60.

XX N-PSDB; AAL44089.

XX New isolated modulator of antigen receptor signalling protein or its
 PT fragment, useful for treating malignant disorders such as myeloid
 PT malignancies, autoimmune disorders and myeloproliferative disorders -

XX Claim 7; Fig 9A; 110pp; English.

XX The invention comprises the amino acid and coding sequences of modulator
 CC of antigen receptor signalling (MARS) proteins. The MARS protein is a
 CC putative tumour suppressor gene and exhibits structural and sequence
 CC similarity to the Src-like adaptor protein (SLAP). The MARS DNA and

CC protein sequences of the invention are useful for the treatment of
 CC myeloid malignancies (e.g. acute myelogenous leukaemia) autoimmune
 CC disorders, immunosuppression, myeloproliferative disorders and
 CC malignancies related to the de-regulation of tyrosine kinases (e.g.
 CC breast cancer). The present amino acid sequence represents a human MARS
 CC protein.

XX Sequence 261 AA;

Query Match 100.0%; Score 446; DB 23; Length 261;
 Best Local Similarity 100.0%; Pred. No. 5.1e-50;
 Matches 83; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 WLVGSLREKAEKELLPGNPGAFILRESQTRGYSLSVRLSPASMDRIIRHYRHL 60
 DB 94 WLVGSLREKAEKELLPGNPGAFILRESQTRGYSLSVRLSPASMDRIIRHYRHL 153
 QY 61 DNGWLYISPRLTFFPSLQALVDHY 83
 DB 154 DNGWLYISPRLTFFPSLQALVDHY 176

RESULT 3

AAU91308
 ID AAU91308 standard; Protein; 261 AA.

XX AAU91308;
 AC
 XX
 DT 18-JUN-2002 (first entry)

XX Human protein NOV13.

XX Human; NOVX; gene therapy; cardiomyopathy; atherosclerosis;
 KW cell signal processing disorder; metabolic pathway modulation disorder;
 KW diabetes; cancer; adenocarcinoma; lymphoma; prostate cancer;
 KW uterus cancer; immune response; graft-versus-host disease;
 KW acquired immunodeficiency syndrome; AIDS; asthma; Crohn's disease;
 KW hypertension; congenital heart defects; multiple sclerosis; inflammation;
 KW Albright hereditary osteodystrophy.

XX Homo sapiens.

XX WO200216599-A2.

XX 28-FEB-2002.

XX 27-AUG-2001; 2001WO-US26510.

XX 25-AUG-2000; 2000US-228191P.

XX 08-FEB-2001; 2001US-267300P.

XX 20-FEB-2001; 2001US-269961P.

XX 20-MAR-2001; 2001US-277337P.

XX (CURA-) CURAGEN CORP.

XX (CORT-) COR THERAPEUTICS INC.

XX Burgess CE, Conley PB, Grosse WJ, Hart M, Kekuda R, Shinkets RA;
 PI Spytek KA, Szekeres ES, Tomlinson JE, Topper JN, Yang R;

XX WPI; 2002-280937/32.

XX N-PSDB; ABR61465.

XX New polypeptides for treating or preventing a disorder associated with
 PT them, in humans, e.g. cardiomyopathy, atherosclerosis or cancers -

XX Claim 3; Page 98; 263pp; English.

XX The invention relates to an isolated polypeptide (NOVX) a mature
 CC form of NOVX, a NOVX variant (differing by no more than 15%), the
 CC nucleotide encoding NOVX (or its complement, fragment or variant).
 CC NOVX is NOV1-14, 15a, 15b, 16a, and 16b. The NOVX polypeptide, nucleic
 CC acid encoding it and antibody against it, are useful for treating or
 CC preventing (e.g. by gene therapy) a NOVX-associated disorder in humans.

CC e.g. cardiomyopathy, atherosclerosis, a disorder related to cell signal
 CC processing and metabolic pathway modulation, diabetes or cancer. The
 CC NOVX polypeptide and nucleic acids are also useful for determining the
 CC presence of predisposition to the diseases. The NOVX nucleic acid and
 CC polypeptide are especially useful in therapeutic or prophylactic
 CC applications for disorders associated with aberrant NOVX expression or
 CC activity, e.g. cancers (e.g., adenocarcinoma, lymphoma, prostate cancer or
 CC uterine cancer), immune response, graft-versus-host disease, acquired
 CC immunodeficiency syndrome (AIDS), asthma, Crohn's disease, hypertension,
 CC congenital heart defects, multiple sclerosis, inflammation or Alzright
 CC hereditary osteodystrophy and many other diseases listed in the
 CC specification. The DNA encoding the protein is useful in gene therapy
 CC for treating the conditions. This is also useful in detection assays,
 CC chromosome mapping, tissue typing, diagnostic or prognostic assays, or
 CC for developing a powerful assay system for functional analysis of
 CC various human disorders, as well as in diagnostic applications. The
 CC present sequence represents a NOVX protein.

CC Sequence 261 AA;

Query Match 100.0%; Score 446; DB 23; Length 261;
 Best Local Similarity 100.0%; Pred. No. 5, 1e-50;
 Matches 83; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 WYEGLSREKAEELLLPGNPGAFILRESQTRGYSLSVRLSPAPMDIRHYRHL 60
 Db 94 WYEGLSREKAEELLLPGNPGAFILRESQTRGYSLSVRLSPAPMDIRHYRHL 153
 Qy 61 DNGWLYISPRITPPSLQALVDHY 83
 Db 154 DNGWLYISPRITPPSLQALVDHY 176

RESULT 4

ID AAB42993 standard; Protein; 248 AA.

AC AAB42993;

XX 08-FEB-2001 (first entry)

DE Human ORFX ORF2757 polypeptide sequence SEQ ID NO:5514.

KW Human; open reading frame; ORFX; detection; cytostatic; hepatotropic;
 KW vulnery; antiproliferative; antiparkinsonian; neurotrophic; neuroprotective;
 KW anticonvulsant; osteoprotective; antiarthritic; immunosuppressant; cardiant;
 KW immunostimulant; thrombolytic; coagulant; vasoregulatory; antidiabetic;
 KW hypotensive; dermatological; immunosuppressive; antineoplastic;
 KW antiviral; antibacterial; antifungal; antipneumatic; antihypertensive;
 KW antianemic; gene therapy; cancer; proliferative disorder; hypertension;
 KW neurodegenerative disorder; osteoarthritis; graft vs host disease;
 KW cardiovascular disease; diabetes mellitus; hypothyroidism; SCID; AIDS;
 KW cholesterol ester storage; systemic lupus erythematosus; infection;
 KW severe combined immunodeficiency; malaria; autoimmune disorder; asthma;
 KW allergy; aplastic anaemia; nocturnal haemoglobinuria; burn; wound;
 KW bone damage; cartilage damage; antiinflammatory disease; coagulation;
 KW thrombosis; contraceptive.

OS Homo sapiens.

PN WO200058473-A2.

XX 05-OCT-2000.

PF 31-MAR-2000; 2000MO-US08621.

XX 31-MAR-1999; 99US-0127607.

PR 02-APR-1999; 99US-0127636.

PR 05-APR-1999; 99US-0127728.

PR 30-MAR-2000; 2000US-0540763.

PA (CURA-) CURAGEN CORP.

PI Shinkens RA, Leach M,
 XX MPI; 2000-602362/57.
 DR N-PSDB; AAC77202.

PT Novel nucleic acids and peptides derived from open reading frame X,
 PT useful for treating e.g. cancers, proliferative disorders,
 PT neurodegenerative disorders and cardiovascular disease -
 XX Claim 11; Page 4693-4694; 5507pp; English.

CC AAC7446 to AAC77606 encode the proteins given in AAB40237 to AAB43397,
 CC which represent the human ORFX open reading frames 1 to 3161. The ORFX
 CC sequences have activities such as: cytostatic; hepatotropic; vulnery;
 CC antiproliferative; antiparkinsonian; neurotrophic; neuroprotective;
 CC osteoprotective; anticonvulsant; antiarthritic; immunosuppressant;
 CC immunostimulant; cardiant; thrombolytic; coagulant; vasoregulatory;
 CC antidiabetic; hypotensive; dermatological; immunosuppressive;
 CC antineoplastic; antibacterial; antiviral; antifungal; antipneumatic;
 CC antihypertensive; and antianemic. The sequences can be used for determining
 CC the presence of or predisposition to, or preventing or treating
 CC pathological conditions associated with an ORFX-associated disorder. The
 CC nucleic acids can be used to express ORFX proteins in gene therapy.
 CC vectors. The proteins and nucleic acids may be used to treat cancers,
 CC proliferative disorders, neurodegenerative disorders, osteoarthritis,
 CC graft vs host disease, cardiovascular disease, diabetes mellitus,
 CC hypertension, hypothyroidism, cholesterol ester storage, systemic lupus
 CC erythematosus, severe combined immunodeficiency (SCID), AIDS, viral,
 CC bacterial or fungal infection, malaria, autoimmune disorders, asthma,
 CC allergies, aplastic anaemia, burns, wounds, bone and cartilage damage,
 CC nocturnal haemoglobinuria, antiinflammatory disease; to enhance
 CC coagulation; to inhibit thrombosis; and as a contraceptive.

XX Sequence 248 AA;

Query Match 99.3%; Score 443; DB 21; Length 248;
 Best Local Similarity 98.8%; Pred. No. 1, 2e-49;
 Matches 82; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 WYEGLSREKAEELLLPGNPGAFILRESQTRGYSLSVRLSPAPMDIRHYRHL 60
 Db 81 WYEGLSREKAEELLLPGNPGAFILRESQTRGYSLSVRLSPAPMDIRHYRHL 140

Qy 61 DNGWLYISPRITPPSLQALVDHY 83
 Db 141 DNGWLYISPRITPPSLQALVDHY 163

RESULT 5

ID AAO15456 standard; Protein; 259 AA.

AC AAO15456;

XX 03-OCT-2002 (first entry)

DE Mouse modulator of antigen receptor signalling (MARS) protein.

KW Mouse; gene therapy; modulator of antigen receptor signalling; MARS;
 KW tumour suppressor gene; Src-like adaptor protein; SLAP;
 KW myeloid malignancy; acute myelogenous leukaemia; autoimmune disorder;
 KW immunosuppression; myeloproliferative disorder; breast cancer.

OS Mus sp.

PN WO200242452-A2.

XX 30-MAY-2002.

PF 26-NOV-2001; 2001WO-CA01662.

PR 27-NOV-2000; 2000CA-2324663.

PA (HOSP-) HOSPITAL FOR SICK CHILDREN.
 XX
 PI Mcglade JC, Loreto MP;
 XX
 DR WPI: 2002-565664/60.
 DR N-PSDB; AAL44087.
 XX
 PT New isolated modulator of antigen receptor signaling protein or its
 PT fragment, useful for treating malignant disorders such as myeloid
 PT malignancies, autoimmune disorders and myeloproliferative disorders -
 XX
 PS Claim 7; Fig 1A; 110pp; English.
 XX
 CC The invention comprises the amino acid and coding sequences of modulator
 CC of antigen receptor signalling (MARS) proteins. The MARS protein is a
 CC putative tumour suppressor gene and exhibits structural and sequence
 CC similarity to the Scr-like adaptor protein (SLAP). The MARS DNA and
 CC protein sequences of the invention are useful for the treatment of
 CC myeloid malignancies (e.g. acute myelogenous leukaemia) autoimmune
 CC disorders, immunosuppression, myeloproliferative disorders and
 CC malignancies related to the de-regulation of tyrosine kinases (e.g.
 CC breast cancer). The present amino acid sequence represents a mouse MARS
 CC protein.
 CC
 SQ Sequence 259 AA;
 XX
 Query Match 92.4%; Score 412; DB 23; Length 259;
 Best Local Similarity 94.0%; Pred. No. 1.5e-45;
 Matches 78; Conservative 1; Mismatches 4; Indels 0; Gaps 0;
 QY 1 WLTYGSLREKAEELLILPCNPGAFILRESQTRRGSYSLVSLSPASWDRIRHYRHCL 60
 DB 93 WLTYGSLREKAEELLILPCNPGAFILRESQTRRGCSYSLVSLSPASWDRIRHYRHCL 152
 QY 61 DNGWLTYSPRLTFPSLQALVDHY 83
 DB 153 DNGWLTYSPRLTFPSLQALVDHY 175
 RESULT 6
 AAB99332
 ID AAB99332 standard; Protein; 505 AA.
 XX
 AC AAB99332;
 XX
 DT 23-AUG-2001 (first entry)
 XX
 DE Human tyrosine kinase Hck protein sequence SEQ ID NO:11.
 XX
 KW Human; tyrosine kinase Hck binding protein; tyrosine kinase; Hck;
 KW tumour lethal factor; tumour necrosis factor alpha; apoptosis; HSB-1;
 KW Hck signal transduction; human immunodeficiency virus; HIV infection;
 KW anticancer.
 XX
 OS Homo sapiens.
 XX
 PN WO200132869-A1.
 XX
 PD 10-MAY-2001.
 XX
 PF 26-OCT-2000; 2000WO-JP07500.
 XX
 PR 29-OCT-1999; 99JP-0309957.
 XX
 PA (SSSE) SSP CO LTD.
 XX
 PI Taniyama T, Narita T;
 XX
 DR WPI, 2001-316440/33.
 XX
 PT New proteins which bind to human tyrosine kinase Hck for promotion of
 PT apoptosis and for the elucidation of the mechanism of Hck signal
 PT transduction -

XX
 PS Example 1; Page 33-35; 45pp; Japanese.
 XX
 CC The present invention describes a protein, designated HSB-1, which binds
 CC to human tyrosine kinase Hck. Also described are: (1) nucleic acids
 CC encoding the protein and its derivatives; (2) recombinant vectors
 CC containing the nucleic acids; and (3) host cells transformed by the
 CC vectors and expressing the protein. HSB-1 has cytostatic activity, binds
 CC tyrosine kinase, enhances tumour necrosis factor alpha and promotes
 CC apoptosis. HSB-1 proteins are used for the elucidation of the mechanism
 CC of Hck signal transduction and of the role of Hck in human
 CC immunodeficiency virus (HIV) infection. They can be used for the
 CC treatment of infections and other diseases with which Hck is associated.
 CC They promote the anticancer activity of tumour necrosis factor alpha.
 CC The present sequence represents the human tyrosine kinase Hck protein,
 CC which is used in an example from the present invention.
 CC
 SQ Sequence 505 AA;
 XX
 Query Match 57.0%; Score 254; DB 22; Length 505;
 Best Local Similarity 57.8%; Pred. No. 1.9e-24;
 Matches 48; Conservative 13; Mismatches 22; Indels 0; Gaps 0;
 QY 1 WLTYGSLREKAEELLILPCNPGAFILRESQTRRGSYSLVSLSPASWDRIRHYRHCL 60
 DB 123 WPKGSLRKDAEROLLAPGMGLSFWIRDSSTTGSISLVDRDPRGDTVKKIRTL 182
 QY 61 DNGWLTYSPRLTFPSLQALVDHY 83
 DB 183 DNGGFLYSPRSTFSTLQELVDHY 205
 RESULT 7
 AAU31072
 ID AAU31072 standard; Protein; 315 AA.
 XX
 AC AAU31072;
 XX
 DT 18-DEC-2001 (first entry)
 XX
 DE Novel human secreted protein #1563.
 XX
 KW Human; vaccination; gene therapy; nutritional supplement;
 KW stem cell proliferation; haematopoiesis; nerve tissue regeneration;
 KW immune suppression; immune stimulation; anti-inflammatory; leukaemia.
 XX
 OS Homo sapiens.
 XX
 PN WO200179449-A2.
 XX
 PD 25-OCT-2001.
 XX
 PF 16-APR-2001; 2001WO-US08656.
 XX
 PR 18-APR-2000; 2000US-0552929.
 XX
 PR 26-JAN-2001; 2001US-0770160.
 XX
 PA (HYSE-) HYSEQ INC.
 XX
 PI Tang YT, Liu C, Drmanac RT;
 XX
 DR WPI, 2001-611725/70.
 XX
 PT Nucleic acids encoding a range of human polypeptides, useful in genetic
 PT vaccination, testing and therapy -
 XX
 PS Claim 20; Page 399; 765pp; English.
 XX
 CC The invention relates to novel human secreted polypeptides. The
 CC polypeptides and antibodies to the polypeptides are useful for
 CC determining the presence of or predisposition to a disease associated
 CC with altered levels of polypeptide. The polypeptides are also useful for
 CC identifying agents (agonists and antagonists) that bind to them. Cells

cc progression at specific boundaries to thereby modulate cell

CC antagonises the hcr SH2 domain without side effects caused by
CC non-specific inhibition of other SH2 domains.

XX Sequence 134 AA;
 SQ Query Match 51.1%; Score 228; DB 17; Length 134;
 Best Local Similarity 54.2%; Pred. No. 9e-22;
 Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;

OY 1 WYEGLSREKAEELLIPGNGCAFLIRESGTSGSYSLVSLRSPASMDRIKRYRHCL 60
 DB 31 WFKNLRSKDAERQLAPGNTGSHFLIRESESTAGSFLSVDFDQNGCEVVKIKIRNL 90

OY 61 DNGWLYISPRLTFFPSLOALVDHY 83
 DB 91 DNGCFYISPRITFFPGLHVLVRYH 113

RESULT 10
 AAM02120
 ID AAM02120 standard; Protein; 134 AA.
 AC AAM02120;
 XX AAM02120;
 DT 28-OCT-1996 (first entry)
 XX DE DDT1-DE2-spacer-ek-lck SH2 construct.
 XX KW Bone resorption disease; osteoporosis; src SH2 domain antagonist;
 XX KW src homology 2 domain; lck SH2 domain.
 XX OS Chimeric Homo sapiens;
 XX OS Chimeric synthetic.

XX FH Key Location/Qualifiers
 FT 2..12
 FT /label= DDT1
 FT /note= "defined epitope tag from HIV-1 gp120/160"
 FT 13..18
 FT /label= DDT2
 FT /note= "hexahistidine tag"
 FT 19..21
 FT /label= Spacer
 FT 22..26
 FT /label= EK
 FT /note= "enterokinase cleavage site"
 FT 27..130
 FT /label= lck-SH2_domain

XX Domain
 XX EP727211-A1.
 XX PN
 XX PD 21-AUG-1996.
 XX PF 07-FEB-1996; 96EP-0200270.
 XX PR 29-DEC-1995; 95US-0580868.
 XX PR 10-FEB-1995; 95US-0386381.
 XX PR 07-MAR-1995; 95US-0400220.
 XX PR 30-JUN-1995; 95US-0497357.
 XX PR 11-OCT-1995; 95US-0541080.
 XX PA (SMIK) SMITHKLINE BEECHAM CORP.
 XX PI Dunnington DJ;
 XX DR WPI; 1996-372674/38.
 XX XX Use of selective src SH2 domain ligand - to prepare medicament for
 PT treating bone resorption disease
 XX PS Example 11; Page 28-29; 47pp; English.
 XX CC Construct DDT1-DE2-spacer-ek-lck SH2 (AAM02120) was obtd. by
 CC inserting a PCR fragment (see also AAT36190-91) coding for human lck
 CC SH2 domain into a vector contg. a tagged chicken src gene

CC DDT1-DE2-spacer-SH2 (see also AAT36186-87). The construct can be
 CC expressed in E. coli and used, together with similar constructs (see
 CC also AAM02119-21 and AAM02124-27), in binding assays to determine the
 CC specificity of cpds. to inhibit SH2 domains; cpds. that selectively
 CC inhibit the human src SH2 domain are useful in treating bone
 CC resorption diseases such as osteoporosis.

XX Sequence 134 AA;
 SQ Query Match 51.1%; Score 228; DB 17; Length 134;
 Best Local Similarity 54.2%; Pred. No. 9e-22;
 Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;

OY 1 WYEGLSREKAEELLIPGNGCAFLIRESGTSGSYSLVSLRSPASMDRIKRYRHCL 60
 DB 31 WFKNLRSKDAERQLAPGNTGSHFLIRESESTAGSFLSVDFDQNGCEVVKIKIRNL 90

OY 61 DNGWLYISPRLTFFPSLOALVDHY 83
 DB 91 DNGCFYISPRITFFPGLHVLVRYH 113

RESULT 11
 AAM11286
 ID AAM11286 standard; peptide; 134 AA.
 AC AAM11286;
 XX AAM11286;
 DT 10-NOV-1997 (first entry)
 XX DE DDT1-DE2-spacer-ek-lck SH2 fusion protein.

XX KW HIV-1; gp120; defined epitope tag; DDT1; envelope protein; human; Stat 6;
 XX KW signal transduction and activation of transcription; src homology 2;
 XX KW signalling molecule; protein tyrosine kinase; oncogenic protein; hep SH2;
 XX KW Gb2 SH2; allergic reaction; erythrocyte production; inhibitor; p85 SH2;
 XX KW asthma; allergic rhinitis; atopic dermatitis; IgE receptor; SH-PTP2 SH2;
 XX KW interleukin-4; IL-4; SH2 domain; Stat5 SH2; lck SH2; fyn SH2;
 XX KW IL-13; therapy; fusion protein.

XX OS Synthetic.
 XX FH Key Location/Qualifiers
 FT 2..12
 FT /note= "defined epitope tag 1 (DDT1)"
 FT 13..18
 FT /note= "defined epitope tag 2 (DDT2)"
 FT 19..21
 FT /note= "spacer"
 FT 22..26
 FT /note= "enteroprotein kinase recognition sequence"
 FT 27..134
 FT /note= "human lck SH2 domain"

XX MO9702023-A1.
 XX PN
 XX PD 23-JAN-1997.
 XX PF 28-JUN-1996; 96WO-US11074.
 XX PR 08-FEB-1996; 96US-0598716.
 XX PR 30-JUN-1995; 95US-0497357.
 XX PA (SMIK) SMITHKLINE BEECHAM CORP.
 XX PI Dunnington DJ;
 XX DR WPI; 1997-108735/10.
 XX XX Treating allergies with specific inhibitor of human Stat 6 SH2
 PT domain - having very low binding affinity to panel of other SH2
 PT domains so free of side effects, specifically for asthma and
 PT allergic rhinitis

XX Example 11; Page 51-52; 88pp; English.

PS
XX
CC AAM11285-W11288 represent fusion proteins containing Src homology 2
CC (SH2) domain. These sequences are used to identify a compound that
CC targets the human Stat (signal transduction and activation of
CC transcription) 6 SH2 domain. The identified compounds have a binding
CC affinity for Stat 6 over 50 (preferably 100) times higher than its
CC affinity for the human Stat5 SH2 domain. The compound has an affinity for
CC hsp SH2, SH-PTP2 SH2, p85 SH2, Grb2 SH2, Ick SH2 or fyn SH2 of
CC more than 50 (preferably 100) times lower than its affinity for Stat 6
CC SH2. SH2 domains are conserved non-catalytic sequences found in a variety
CC of signalling molecules, such as non-receptor protein tyrosine kinases,
CC and in oncogenic proteins. The compounds identified using the fusion
CC proteins are used as the administered compound in the method of the
CC invention for treating allergic reactions. Administration of the compound
CC avoids the side effects (e.g. reduced erythrocyte production) associated
CC with non-selective inhibition of SH2 domains. Selective compounds can be
CC identified in competitive binding assays using only a small subset (the
CC domains specified above) of SH2 domains rather than all 60 known
CC domains. The method can be used for the treatment of asthma and allergic
CC rhinitis, but can also be used to treat atopic dermatitis. Inhibition of
CC the human Stat 6 SH2 domain blocks up-regulation of the IgE receptor
CC mediated by interleukin-4 (IL-4) or IL-13.

XX Sequence 134 AA;

Query Match 51.1%; Score 228; DB 18; Length 134;
Best Local Similarity 54.2%; Pred. No. 9e-22;
Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;

QY 1 WYEGLSREKAEELLILPQNGAFLIRSGSYSLSVRLSPASMDRIHRYHCL 60
DB 31 WFKNLRSKDAERQLAPGNTGSGFLIRSESTAGSPSLVDPQNGEVVHYKIRNL 90

QY 61 DNGMWLYSPRLTPPSLOALVDHY 83
DB 91 DNGGFYISPRITTPGLHVLRYH 113

RESULT 12

ID AAM19624 standard; Protein; 134 AA.

AC AAM19624;

DT 27-OCT-1997 (first entry)

XX Human Ick SH2 domain fusion protein.

XX Stat 5; Signal Transduction and Activation of Transcription;
XX Src homology domain; SH2; erythropoiesis enhancing; anaemia;
XX fusion protein; ek; enterokinase; epitope; antibody production;
XX detection; HIV; human immunodeficiency virus type 1; gp120;
XX glycoprotein 120; selective.

OS Homo sapiens.

XX Key Location/Qualifiers

FT Peptide 2..12 /note= "defined epitope tag 1 from HIV gp120"

FT Peptide 13..18 /note= "hexahistidine sequence tag"

FT Region 19..21 /label= spacer

FT Cleavage-site 22..26 /note= "enterokinase protease recognition site"

FT Peptide 27..134 /note= "Ick SH2"

PN MO9702024-A1.

XX 23-JAN-1997.

XX 28-JUN-1996; 96WO-US11158.

XX 08-FEB-1996; 96US-0598715.

XX 30-JUN-1995; 95US-0497357.

XX (SMK) SMITHKLINE BEECHAM CORP.

XX Dunnington DJ;

XX WPI; 1997-108736/10.

XX Enhancing erythropoiesis with specific activator of human Stat 5 SH2

XX domain - has very low binding affinity to other SH2 domains so free

XX of side effects, particularly for treating anaemia

XX Example 11; Page 54-55; 91pp; English.

XX AAM19624 is a fusion protein of formula DET1-DET2-SP-ek-SH2, where
XX DET1 is a defined epitope tag from HIV-1 gp120, DET2 is a hexahistidine
XX sequence tag (binds to nickel-containing resins, used for purification),
XX SP is a spacer, ek is an enterokinase protease recognition site and SH2
XX is the human Ick SH2 domain. DET1 is included so that antibodies
XX against the epitope can be used to detect the recombinant expression
XX of the fusion protein and hence the SH2 domain. The fusion proteins
XX are used for identifying compounds that bind the SH2 domain causing
XX its activation.

XX Sequence 134 AA;

Query Match 51.1%; Score 228; DB 18; Length 134;
Best Local Similarity 54.2%; Pred. No. 9e-22;
Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;

QY 1 WYEGLSREKAEELLILPQNGAFLIRSGSYSLSVRLSPASMDRIHRYHCL 60
DB 31 WFKNLRSKDAERQLAPGNTGSGFLIRSESTAGSPSLVDPQNGEVVHYKIRNL 90

QY 61 DNGMWLYSPRLTPPSLOALVDHY 83
DB 91 DNGGFYISPRITTPGLHVLRYH 113

RESULT 13

ID AAM14788 standard; Protein; 224 AA.

AC AAM14788;

DT 20-JUN-1997 (first entry)

XX FKBP-LCK:SH2 fusion protein.

XX FKBP-LCK:SH2; FK506 binding protein; SH2 domain; Src homology 2;
XX fusion protein; high throughput assay; signal transduction; ligand;
XX microcirculation.

OS Homo sapiens.

XX Key Location/Qualifiers

PN WO9710253-A1.

PD 20-MAR-1997.

PF 11-SEP-1996; 96WO-US14567.

PR 12-MAR-1996; 96GB-0005210.

PR 15-SEP-1995; 95US-0003819.

XX (MERI) MERCK & CO INC.

XX Marcy A, Salowe SP, Wisniewski D;

XX WPI; 1997-202171/18.

DR N-PSDB; AAT63421.
 XX Screening compounds for binding to fusion proteins with defined
 PT ligands - allows high capacity assays and identification of
 PT (ant)agonists or inhibitors for drug development
 XX
 PS Claim 32; Page 21-22; 36pp; English.
 CC Novel fusion proteins FKBP-ZAP:SH2, FKBP-SYK:SH2 and FKBP-LCK:SH2
 CC (AAM14766-88) comprise FK506 binding protein (FKBP) linked via a
 CC peptide linker to a target protein composed of a multiple signal
 CC transduction domain, i.e. ZAP:SH2, SYK:SH2 or LCK:SH2. They can
 CC be produced in transformed host cells, esp. E. coli, using
 CC expression vectors with fusion protein DNA sequences (AAT63419-21).
 CC The fusion proteins are used in novel methods utilising
 CC microscintillation plate technology for the functional assay of
 CC ligand binding to a signal transduction domain (i.e. SH2). The
 CC method is readily adaptable to robotic automation for high
 CC capacity screening for agonists, antagonists and/or inhibitors
 CC for use in drug development.
 CC
 CC Sequence 224 AA;
 SQ
 Query Match 51.1%; Score 228; DB 18; Length 224;
 Best Local Similarity 54.2%; Pred. No. 1.7e-21;
 Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;
 Oy 1 WLVEGLSRKAEKELLIPGNGCAFILRESQTRRGSSVLSVLRPSAMDRIRHYRHL 60
 Db 125 WFKNLSRKDAERQLAPGNTGHSFLRSESTAGSFSLVRDPDQNGEVKHKIRNL 184
 Oy 61 DNGWLTVISPRLTFFPSLQALVDHY 83
 Db 185 DNGGFYISPRITFPGLHELVRYH 207
 RESULT 14
 AAW96823
 ID AAW96823 standard; Protein; 224 AA.
 XX
 AC AAW96823;
 XX
 DT 21-APR-1999 (first entry)
 XX
 DE A fusion protein of FKBP-Lck.
 XX
 KW Fusion protein; FK506 binding protein; FKBP; SH2 domain; human Lck;
 KW screening; protein binding; ligand-protein interaction;
 KW protein-protein interaction; protease inhibitor.
 XX
 OS Synthetic.
 OS Homo sapiens.
 XX
 PN WO9841866-A1.
 XX
 PD 24-SEP-1998.
 XX
 PF 10-MAR-1998; 98WO-US04610.
 XX
 PR 14-MAR-1997; 97US-0040795.
 XX
 PA (MERI) MERCK & CO INC.
 XX
 PI Hermes JD, Salowe SP, Sinclair EU;
 XX
 DR WPI; 1999-070061/06.
 DR N-PSDB; AAX15151.
 XX
 PT High throughput screening assay - for screening compounds capable of
 PT binding to a fusion protein consisting of, e.g., a target protein
 PT and an FK506-binding protein.
 XX
 PS Disclosure; Page 26; 42pp; English.

XX
 CC The present sequence represents a fusion protein comprising FK506 binding
 CC protein (FKBP) and the SH2 domain of human Lck. The protein is used
 CC to exemplify the method of the invention. The specification describes a
 CC method for screening for compounds capable of binding to a fusion
 CC protein. The method comprises mixing a test compound, a biotinylated
 CC ligand, the fusion protein, a donor-labelled ligand and acceptor-labelled
 CC streptavidin. Incubating the mixture, measuring the time-resolved
 CC fluorescence attributable to the binding of the biotinylated ligand
 CC to the fusion protein in the presence of the test compound and
 CC determining the binding of the biotinylated ligand to the fusion protein
 CC in the presence of the test compound relative to a control assay run in
 CC the absence of the test compound. The methods may be used to determine
 CC if compounds are capable of binding to a protein or are capable of
 CC blocking ligand-protein or protein-protein interactions. They may be
 CC used to identify compounds which are protease inhibitors.
 CC
 CC Sequence 224 AA;
 SQ
 Query Match 51.1%; Score 228; DB 20; Length 224;
 Best Local Similarity 54.2%; Pred. No. 1.7e-21;
 Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;
 Oy 1 WLVEGLSRKAEKELLIPGNGCAFILRESQTRRGSSVLSVLRPSAMDRIRHYRHL 60
 Db 125 WFKNLSRKDAERQLAPGNTGHSFLRSESTAGSFSLVRDPDQNGEVKHKIRNL 184
 Oy 61 DNGWLTVISPRLTFFPSLQALVDHY 83
 Db 185 DNGGFYISPRITFPGLHELVRYH 207
 RESULT 15
 AAB37700
 ID AAB37700 standard; protein; 508 AA.
 XX
 AC AAB37700;
 XX
 DT 02-MAR-2001 (first entry)
 XX
 DE Human lymphocyte kinase.
 XX
 KW Human lymphocyte kinase; protein co-ordinate data; lck; crystal.
 KW Homo sapiens.
 XX
 OS
 OS WO200070030-A1.
 XX
 PD 23-NOV-2000.
 XX
 PF 19-MAY-2000; 2000WO-US13881.
 XX
 PR 19-MAY-1999; 99US-0134965.
 XX
 PA (KINE-) KINETIX PHARM INC.
 XX
 PI Zhu X;
 XX
 DR WPI; 2000-687708/67.
 XX
 PT Crystal of a protein-ligand complex for identifying kinase inhibitors,
 PT comprising a truncated lymphocyte kinase and a ligand, and diffracts
 PT X-rays to determine atomic coordinates at a resolution greater than 5
 PT angstroms -
 XX
 PS Claim 1; Page 434-5; 438pp; English.
 XX
 CC The present invention relates to a crystal of a protein-ligand complex
 CC comprising a truncated lymphocyte kinase (lck) and a ligand. The crystal
 CC diffracts X-rays so that the atomic coordinates of the protein-ligand
 CC complex can be determined to a resolution of greater than 5.0 Angstroms.
 CC The truncated lck used in the present invention comprises the globular
 CC core of the corresponding full-length lck. The present sequence is the

full-length human Ick protein. The crystal of the present invention may be used to identify kinase inhibitors in screening assays in drug screening and drug design processes, to design select or test inhibitors of kinase enzymes, where the inhibitors are used as therapeutics for the treatment and modulation of diseases, disease symptoms or the effect of other physiological events mediated by kinases, having one or more kinase enzymes involved in their pathology.

SQ Sequence 508 AA;

Sequence 508 AA;

Query Match	51.1%;	Score 228;	DB 21;	Length 508;
Best Local Similarity	54.2%;	Pred. No. 5e-21;		

Matches 45; Conservative 12; Mismatches

Matches 45; Conservative 12; Mismatches 26; Indels 0; Gaps 0;

QY 1 WLVEGLSREKAEEILLIPGNPGAFLLIESQTGRGSYSIVLSRPAIMDRIRHYRIHL 60
|::|||::|||::|||::|||::|||::|||::|||::|||::|||::|||::|||::|||
Db 126 WFFKNLSRKDAERQLAPGNTHSFLIESESTAGSFSLSVRPFDQNGCEVVKHKINL 185

Db 126 WFFKNLSRKDAERQLAPGNTGHSFLIRESESTAGSFSLSYRDPDQNGEYVVKHYKIRNL 185

QY 61 DNGWLYISPRLTFFSLQALVDHY 83

Db 186 DNGGFYISPRITFPGLHELVRHY 208

Search completed: March 24, 2003, 15:48:37
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